Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–594–0095.

SUPPLEMENTARY INFORMATION: FDA is announcing the availability of a draft guideline entitled ''Draft Guideline on the Manufacture of Positron Emission Tomographic (PET) Drug Products.'' PET is a diagnostic imaging modality consisting of onsite production of radionuclides that are intravenously injected into patients for diagnostic purposes. The potential usefulness of a PET radiopharmaceutical is based upon the product's interaction with a biochemical process in the body. For example, the product may be substituted for glucose in anaerobic glycolysis, theoretically localizing in ischemic tissues where glucose metabolism is the predominant energy source (epileptic foci, acute vascular insufficiency states).

The manufacture of PET radiopharmaceuticals consists of a process that takes place within a few hours. A target material is irradiated by a cyclotron; chemical synthesis takes place in a programmed, automated apparatus; and the final solution is compounded and filled. The biological distribution of a PET radiopharmaceutical in the body is monitored by a positron tomograph, or PET scanner, which detects the photons emitted as a result of the radioactive decay of the PET radiopharmaceutical. Because of their short half-lives, PET radiopharmaceuticals are characteristically manufactured in PET centers in response to daily demand for relatively few patients. PET centers are usually located in medical centers.

PET manufacturing procedures differ in a number of important ways from those associated with the manufacture of conventional drug products, mainly due to the short half-lives involved:

1. A maximum of only a few lots are manufactured per day, with one lot equaling one multiple-dose vial. This is administered to the patient usually within a matter of hours. Prolonged manufacturing time significantly erodes the useful clinical life of PET radiopharmaceuticals.

2. The quantities of radioactive active ingredients contained in each lot of a PET radiopharmaceutical generally vary from nanogram to milligram amounts, depending upon various product parameters.

3. Because one lot equals one multiple-dose vial containing a homogeneous solution of a PET product (e.g., 2-deoxy-2 [^{18}F]fluoro-D-glucose), results from end-product testing of samples drawn from the single vial have the maximum possible probability of being representative of all the doses administered to patients from that vial, barring sampling or testing error.

4. An entire lot may be administered to one or several patients, depending upon the activity remaining in the container at the time of administration. Consequently, the administration of the entire quantity of a lot to a single patient should be anticipated for every lot manufactured. This is an important consideration when establishing the testing limits for certain attributes such as endotoxins and impurities.

5. PET radiopharmaceuticals usually do not enter a general drug distribution chain. Rather, the entire lot (one vial) is usually distributed directly from the PET center either to a single medical department or physician for administration to patients or to a radiopharmacy for dispensing. Distribution may occur to other centers when the geographic proximity will allow for distribution and use within the drug product's half-life parameters.

Conventional compliance with CGMP regulations would be expected where special characteristics such as those listed above do not exist; for example, in large-scale PET operations. Elsewhere in this issue of the Federal Register, FDA is publishing (1) A proposed rule that would authorize the Director, CDER, or the Director, Office of Compliance, CDER, to approve exceptions or alternatives to the application of the provisions of 21 CFR part 211 to the manufacture of PET radiopharmaceuticals, and (2) a notice of a public workshop and FDA guidance on the regulation of PET radiopharmaceuticals.

The guideline entitled ''Draft Guideline on the Manufacture of Positron Emission Tomographic (PET) Drug Products'' discusses, generally, quality control units, personnel qualifications, staffing, buildings and facilities, equipment, components, containers, closures, production and process controls, packaging and labeling control, holding and distribution, testing and release for distribution, stability testing and expiration dating, reserve samples, yields, second-person checks, and reports and records.

FDA is making this draft guideline available for public comment before issuing a final guideline. If, following the receipt of comments, the agency concludes that the draft guideline will assist persons in determining whether manufacturing practices used in the small-scale production of liquid injectable PET radiopharmaceuticals are in compliance with FDA's CGMP regulations for finished pharmaceuticals, then the agency will prepare a final guideline and will announce its availability in the Federal Register.

Guidelines are generally issued under § 10.90(b) (21 CFR 10.90(b)), which provides for the use of guidelines to state procedures or standards of general applicability that are not legal requirements but are acceptable to FDA. The agency is now in the process of revising § 10.90(b). Therefore, if the agency makes the guideline final, the guideline would not be issued under the authority of current § 10.90(b), and would not create or confer any rights, privileges, or benefits for or on any person, nor would it operate to bind FDA in any way.

Interested persons may, on or before May 30, 1995, submit to the Dockets Management Branch (address above) written comments on the draft guideline. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The draft guideline and received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: February 17, 1995.

William B. Schultz,

Deputy Commissioner for Policy.

[FR Doc. 95–4689 Filed 2–24–95; 8:45 am]

BILLING CODE 4160–01–F

[Docket No. 93N–0005]

Regulation of Positron Emission TomographyRadiopharmaceutical Drug Products; Guidance; Public Workshop

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is publishing guidance on the regulation of positron emission tomography (PET) radiopharmaceutical drug products. FDA has developed this guidance to make clear the regulatory approach designed to help ensure the safe and effective use of these products. The agency is also announcing a public workshop to facilitate an understanding of regulatory requirements regarding these products.

DATES: The public workshop will be held on March 21, 1995, 8:30 a.m. to 4 p.m. Registration will be between 8 a.m. and 8:30 a.m. Due to limited space, interested persons must preregister before March 7, 1995, by telephoning

the contact person listed below. Interested persons may submit data, information, or views on this subject to the Dockets Management Branch (address below).

ADDRESSES: The public workshop will be held at the Parklawn Bldg., conference rooms G and H, 5600 Fishers Lane, Rockville, MD 20857. Written data, information, or views regarding the workshop may be submitted to the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: John W. Levchuk, Center for Drug Evaluation and Research (HFD–322), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–594–0095.

SUPPLEMENTARY INFORMATION:

I. Background

PET is a diagnostic imaging modality consisting of onsite production of radionuclides that are usually intravenously injected into patients for diagnostic purposes. The potential usefulness of a PET radiopharmaceutical is based upon the product's interaction with a biochemical process in the body. For example, the product may be substituted for glucose in anaerobic glycolysis, theoretically localizing in ischemic tissues (epileptic foci, acute vascular insufficiency states) where glucose metabolism is the predominant energy source.

The manufacture of PET radiopharmaceuticals consists of a process that takes place within a few hours. A target material is irradiated in a cyclotron; chemical synthesis takes place in a programmed, automated apparatus; and the final solution is prepared. The biological distribution of a PET radiopharmaceutical in the body is monitored by a positron tomograph, or PET scanner, which detects the photons emitted as a result of the radioactive decay of the PET radiopharmaceutical.

Currently, there are two FDA approved PET radiopharmaceuticals: Rubidium-82 (rubidium chloride ([^{82}Rb]RbCl)) and fludeoxyglucose (^{18}-F-FDG). At present, most investigational PET radionuclides are manufactured by cyclotrons at PET facilities, which generally are located at major teaching hospitals or their adjacent universities. Because PET radiopharmaceuticals contain positron emitting isotopes that have relatively short half-lives (minutes to hours), they are manufactured near the site of administration to patients. Products may be distributed t o other institutions when the geographic proximity of these locations will allow for distribution and use within the product's half-life parameters.

The development of PET radiopharmaceuticals has increased considerably over the past several years. As this technology has advanced, questions have been raised about the most appropriate approach to regulation of PET radiopharmaceuticals. FDA held a public hearing on March 5, 1993, to receive information and views on this issue from interested groups and individuals. The docket established for the receipt of comments (Docket No. 93N–0005) remained open for an additional 2 weeks after the hearing.Additionally, FDA has received several citizen petitions on PET radiopharmaceuticals to which it will be directly responding.

Having considered the available information, including that presented to the agency at the hearing and in written materials, FDA has concluded that radiopharmaceuticals should be regulated under the drug provisions of the Federal Food, Drug, and Cosmetic Act (the act). Under section 501(a)(2)(B) of the act (21 U.S.C. 351(a)(2)(B)), drugs are considered adulterated unless manufactured in conformity with current good manufacturing practice (CGMP). Because of unique features of PET radiopharmaceuticals, the applicability of certain requirements in the CGMP regulations for finished pharmaceuticals (part 211 (21 CFR part 211)) to PET radiopharmaceuticals may differ from the applicability of these requirements to drugs produced through traditional manufacturing methods. Consequently, elsewhere in this issue of the Federal Register, FDA is publishing a proposed rule that would authorize the Director of the Center for Drug Evaluation and Research (CDER) or the Director of the Office of Compliance, CDER, to approve exceptions or alternatives to the application of the provisions of part 211 to the manufacture of PET radiopharmaceuticals.

In order to assist manufacturers in complying withapplicable CGMP requirements, FDA has also developed a ''Draft Guideline on the Manufacture of Positron Emission Tomographic (PET) Drug Products.'' A notice of availability of this draft guideline, on which the agency is inviting comments, is also published elsewhere in this issue of the Federal Register.

Under section 505 of the act (21 U.S.C. 355), ''new drugs,'' such as radiopharmaceuticals, must be the subjects of approved new drug applications (NDA's) or abbreviated new drug applications (ANDA's) before marketing. In order to be approved, the products must be shown to be safe and effective for their intended uses through adequate and well-controlled studies (21 U.S.C. 355(d)). Investigational use of drug products is governed, in general, by the requirements in part 312 (21 CFR part 312). Special provisions concerning radioactive drugs for certain research uses are contained in FDA regulations at 21 CFR 361.1. Under these special provisions, use of radioactive drug products in human subjects during the course of limited kinds of research projects may occur if the use is approved by a properly constituted Radioactive Drug Research Committee and if other conditions are met.

Section 502 of the act (21 U.S.C. 352) sets forth misbranding provisions applicable to drug products. Among other circumstances, a drug is considered misbranded if the product labeling is false or misleading or if the drug is dangerous to health when used as suggested in the labeling (21 U.S.C. 352(a) and (j)). For prescription drugs, section 502(n) of the act describes certain information that must be included in all advertisements or other printed materials. FDA's regulations also establish labeling and advertising requirements in more detail (21 CFR parts 201 and 202).

Section 510 of the act (21 U.S.C. 360) requires persons who own or operate establishments for the manufacture, preparation, propagation, compounding, or processing of drugs (with certain exceptions) to register the establishments with FDA. Individuals who must register their establishments under section 510 of the act must also file a list of all the drugs being made or processed at the establishment. Drug registration and listing regulations are codified at part 207 (21 CFR part 207).

II. Guidance: Regulation of PET Radiopharmaceuticals

FDA regulates PET radiopharmaceutical drug products used in purely physiologic research, where the results of such research are not used to guide patient management or treatment decisions, as well as in investigational clinical trials and clinical practice. All facilities that manufacture PET radiopharmaceuticals must be registered with FDA in accordance with FDA regulations on the registration and listing of producers of drugs (part 207). Facilities that manufacture PET radiopharmaceuticals are not exempt from registration under §1A207.10 because their activities do not fall within the scope of the regular course of the practice of the profession of pharmacy. This policy statement

supersedes the ''Nuclear Pharmacy Guideline; Criteria for Determining When to Register as a Drug Establishment'' issued by FDA in May 1984.

A. Physiological Research

Facilities using PET radiopharmaceuticals for purely physiological research, where the results of such research are not used to guide patient management or treatment decisions, should establish a PET Regulatory Committee (PRC) in accordance with §1A361.1 *Radioactive drugs for certain research uses* (21 CFR 361.1). The PRC will monitor all physiological research of the PET facility. Facilities using PET radiopharmaceuticals for purely physiological research are not required to submit an investigational new drug application (IND) or NDA as long as this research is intended to obtain basic information regarding metabolism or physiology and is not intended to guide or be part of therapeutic, diagnostic, or clinical management plans.

FDA will approve and monitor the PRC, which should consist of at least five individuals. In accordance with §1A361.1(c), each PRC should include: (1) A physician recognized as a specialist in nuclear medicine; (2) a person qualified by training and experience to manufacture PET radiopharmaceuticals; and (3) a person with special competence in radiation safety and radiation dosimetry. The remaining PRC members should include individuals qualified in various disciplines pertaining to the field of nuclear medicine, and should be sufficiently diverse to permit expert review of the technical and scientific aspects of proposals submitted to the committee. In addition to the requirements in §1A361.1(c) and with the exception of the member qualified by training and experience to manufacture PET radiopharmaceuticals, PRC membership should include a representative of a consumer group, and the members should not have scientific, clinical, financial, or administrative conflicts of interest.

The PRC should have three main responsibilities: (1) To approve research protocols; (2) to prepare annual reports; and (3) to determine when purely physiological research has ended.

In approving protocols, the PRC should: (1) Determine if the investigator meets the qualifications specified in the protocol; (2) review the research protocol design; (3) review and monitor the selection of research subjects; (4) ensure that the research subjects have signed informed consent documents; (5) review and monitor the quality of the PET radiopharmaceuticals administered; (6) evaluate all reports of adverse events; and (7) confirm concurrence of Institutional Review Board approval.

The annual report should follow the format and contents prescribed in §1A361.1(c)(3), summarizing the conditions of use, doses, route of administration, protocols, adverse events reported in the safety information, and the chemistry, manufacturing, and control data. The PRC should submit the completed annual report to FDA.

The PRC is also responsible for determining when purely physiological research becomes investigational clinical use. This determination should be based on whether the data obtained will be used in the diagnostic, therapeutic, or clinical management of patients. Once trials are proposed for investigational clinical use, the facility must submit an IND before starting to conduct the trials.

B. Investigational Use

Manufacturers of PET radiopharmaceuticals intended to be used in investigational clinical trials must submit an IND to FDA in accordance with the regulations in part 312. Institutions or investigators working together with the same PET radiopharmaceutical may submit one IND for that drug product, covering studies conducted at more than one site or institution.

C. NDA Approval

Submission of an NDA, in accordance with FDA regulations in part 314 (21 CFR part 314), is required for PET radiopharmaceuticals used in clinical practice. Institutions or investigators working together with the same PET radiopharmaceutical may submit one NDA for that drug product. All sites that produce the same drug product would be covered by the submitted NDA. Once an NDA is approved, other PET facilities with a radiopharmaceutical that is an equivalent finished product, but which did not participate in the NDA or did not submit manufacturing data, could submit an abbreviated new drug application (ANDA) demonstrating that their drug is bioequivalent to the innovator drug, in accordance with FDA regulations in part 314. Alternatively, the NDA holder could submit a supplement to add these other facilities as new manufacturing sites.

PET radiopharmaceuticals are also subject to the adulteration and misbranding provisions of the act. Facilities where PET radiopharmaceuticals are manufactured are subject to inspection by FDA for compliance with CGMP requirements and other drug-related requirements.

Dated: February 17, 1995.

William B. Schultz,

Deputy Commissioner for Policy.

[FR Doc. 95–4691 Filed 2–24–95; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

Office of the Assistant Secretary for Public and Indian Housing

[Docket No. N–55–3710; FR–3636–-03]

Announcement of Funding Awards Public Housing Drug Elimination Technical Assistance Program, FY 1994

AGENCY: Office of the Assistant Secretary for Public and Indian Housing, HUD.

ACTION: Announcement of funding awards.

SUMMARY: In accordance with section 102(a)(4)(C) of the Department of Housing and Urban Development Reform Act of 1989, this announcement notifies the public of funding decisions made by the Department in a competition for funding under the Notice of Funding Availability (NOFA) for Public Housing Drug Elimination-Technical Assistance Program. This announcement contains the names and addresses of the award winners and the amount of the awards.

FOR FURTHER INFORMATION CONTACT: Elizabeth Cocke, Drug Free Neighborhoods Division, Department of Housing and Urban Development, 451 Seventh Street, SW., Room 4116, Washington, DC 20410, telephone (202) 708–1197. A telecommunications device for hearing or speech impaired persons (TDD) is available at (202) 708–0850. (These are not toll-free numbers.)

SUPPLEMENTARY INFORMATION: The Public Housing Drug Elimination-Technical Assistance Program is authorized by the Departments of Veterans Affairs and Housing and Urban Development, and Independent Agencies Appropriations Act, 1994 (approved October 28, 1993, Pub. L. 103–124).

The NOFA published in the Federal Register on March 10, 1994 (59 FR 11418) announced the FY 1994 availability of $1,255,175 to fund qualified applicants selected under the FY 1993 NOFA and invited additional applicants for FY 1994. The purpose of